Persistent autonomic dysfunction following mild COVID-19: evidence from the orthostatic heart rate variability response

Disfunção autonômica persistente após COVID-19 leve: evidências da resposta ortostática da variabilidade da frequência cardíaca

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Abstract

Introduction: Autonomic alterations following COVID-19 have been reported in individuals with mild disease.
Objective: To investigate long-term effects of non-hospitalized COVID-19 on cardiovascular autonomic regulation, focusing on heart rate variability (HRV), blood pressure variability (BPV), and baroreflex sensitivity (BRS).
Methodology: Eighty-five sedentary men aged 35–55 were allocated to CONTROL group (n = 43), assessed before the COVID-19 pandemic, and COVID-19 group (n = 42), evaluated at least six months after SARS-CoV-2 infection. Continuous recordings of heart rate and blood pressure were obtained in the supine position and during active standing. HRV, BPV, and BRS were analyzed using linear, nonlinear methods.
Results: Anthropometric and baseline hemodynamic variables did not differ between groups. In the supine position, HRV indices were comparable, except for approximate entropy in the COVID-19 group (1.46 ± 0.14 vs. 1.35 ± 0.13; p = 0.020). During orthostasis, the COVID-19 group showed reduced low-frequency (LF) oscillations of HRV (70 ± 17 vs. 81 ± 10%; p < 0.001), a lower LF/high-frequency ratio (4.12 ± 3.70 vs. 6.7 ± 4.4; p < 0.001), and decreased SD2 (standard deviation of long-term variability) from the Poincaré plot (45 ± 14 vs. 51 ± 19 ms; p = 0.048). BPV, BRS responses to postural stress were similar between groups.
Discussion: These findings indicate that individuals recovered from mild COVID-19 present subtle, persistent alterations in heart rate dynamics during postural challenge, suggesting incomplete autonomic adjustment to physiological stress.
Conclusion: Mild COVID-19 may be associated with persistent autonomic alterations during physiological stress.

Keywords

Baroreflex sensitivity; cardiovascular autonomic control; COVID-19; heart rate variability.

Resumen

Introdução: Alterações autonômicas após a COVID-19 têm sido descritas em indivíduos com doença leve.
Objetivos: Investigar efeitos persistentes da COVID-19 leve sobre a regulação autonômica cardiovascular, através da variabilidade da frequência cardíaca (VFC) e da pressão arterial (VPA) e na sensibilidade do barorreflexo (SBR).
Métodos: 85 homens sedentários, entre 35 e 55 anos, foram alocados nos grupos CONTROLE (n = 43), avaliado antes da pandemia de COVID-19, e COVID-19 (n = 42), avaliado pelo menos seis meses após infecção por SARS-CoV-2. Registros contínuos da frequência cardíaca e da pressão arterial foram obtidos nas posições supina e durante ortostatismo ativo.
Resultados: Variáveis antropométricas e hemodinâmicas basais não diferiram entre os grupos. Na posição supina, os índices de VFC foram semelhantes, exceto a entropia aproximada, maior no grupo COVID-19 (1,46 ± 0,14 vs. 1,35 ± 0,13; p = 0,020). Em ortostatismo, o grupo COVID-19 apresentou menores oscilações de baixa frequência da VFC (70 ± 17 vs. 81 ± 10%; p < 0,001) razão LF/alta frequência (4,12 ± 3,70 vs. 6,7 ± 4,4; p < 0,001) e SD2 (desvio padrão da variabilidade em longo prazo) do gráfico de Poincaré (45 ± 14 vs. 51 ± 19 ms; p = 0,048). As respostas de VPA e SBR ao estresse postural foram semelhantes entre os grupos.
Discussão: Esses achados indicam que indivíduos recuperados da COVID-19 leve apresentam alterações persistentes sutis na dinâmica da frequência cardíaca durante mudança postural, sugerindo ajuste autonômico incompleto.
Conclusão: COVID-19 leve pode estar associada a alterações autonômicas persistentes durante estresse fisiológico.

Palavras chave

Controle autonômico cardiovascular; COVID-19; sensibilidade barorreflexa; variabilidade da frequência cardíaca.

Introduction

The autonomic nervous system (ANS) plays a pivotal role in regulating cardiovascular function, continuously adapting to the demands imposed by a wide range of physiological conditions (Gibbons, 2019; Wehrwein et al., 2016). In addition, it interacts with other physiological systems to maintain overall homeostasis. However, the presence of acute or chronic diseases can disrupt this regulation, impairing the efficiency of the ANS and negatively affecting its modulatory capacity (Bairey Merz et al., 2015; Gibbons, 2019; Wehrwein et al., 2016).

In this context, beyond its well-documented respiratory manifestations, infection with SARS-CoV-2 has been shown to affect multiple body systems, including the ANS. Evidence suggests that the neurotropic characteristics of the virus, along with its ability to invade the central nervous system, may increase the susceptibility of the ANS to dysfunction (Yachou et al., 2020). This susceptibility has been reflected in significant alterations in the autonomic modulation of heart rate variability (HRV), particularly during the acute phase of infection and in individuals experiencing long COVID, which is characterized by persistent impairments in cardiovascular autonomic control (Al-kuraishy et al., 2021; Asarcikli et al., 2022; Dani et al., 2021; Idris Fadul et al., 2025).

However, the ANS is not solely responsible for regulating heart rate (HR). In this context, studies involving hospitalized COVID-19 patients have reported an association between increased blood pressure variability (BPV) and unfavorable clinical outcomes (Jagannatha et al., 2023; Nam et al., 2021). Moreover, there is evidence of persistent impairments in baroreflex sensitivity (BRS) accompanied by carotid stiffness in these individuals (Cairo et al., 2025; Srivastava et al., 2023). Although these studies were conducted in hospitalized individuals, they provide important insight into the potential pathways through which SARS-CoV-2 may disrupt autonomic regulation. Because intact autonomic regulation of BRS and BPV is essential for performing daily activities, these disturbances may render even simple tasks, such as transitioning to an upright posture, unexpectedly challenging (Ding et al., 2020; Zhang et al., 2004).

Nevertheless, the long-term effects of mild COVID-19 cases on cardiovascular autonomic modulation remain poorly understood. This gap in knowledge is of clinical concern, as disturbances in autonomic cardiovascular regulation are considered important risk factors for the development and progression of cardiovascular disease. Therefore, it is essential to investigate the integrity of autonomic control in individuals with a history of SARS-CoV-2 infection.

Accordingly, the aim of the present study was to investigate the long-term effects of COVID-19 on cardiovascular autonomic parameters, with a particular focus on the autonomic modulation of HRV, BPV, and BRS.

Method

Sampling

Eighty-five sedentary men aged between 35 and 55 years were allocated into two groups: the CONTROL group (n = 43), consisting of participants from previous studies conducted by the same research team before the COVID-19 pandemic, and the COVID-19 group (n = 42), composed of individuals diagnosed with SARS-CoV-2 via serological or antigen testing at least six months prior to the assessments. All participants in the COVID-19 group reported experiencing symptoms such as fever, nasal discharge, dry cough, and sneezing, but none required hospitalization.

Assessments were conducted in a single morning session (between 7:00 and 11:00 AM) at the Exercise Physiology and Cardiovascular Physiotherapy Laboratory of the Ribeirão Preto Medical School, University of São Paulo. Anthropometric measurements, cardiorespiratory fitness testing using a cardiopulmonary exercise test, and continuous recordings of HR and blood pressure were performed for analysis of HRV, BPV, and BRS. Participants in both groups were recruited through media advertisements and social media platforms. All participants provided written informed consent. The study was approved by the Research Ethics Committee of the University Hospital, Ribeirão Preto Medical School, University of São Paulo (Process No. 5.651.063/2022).

Exclusion Criteria

To minimize confounding, smokers and individuals with acute or chronic-degenerative conditions (e.g., hypertension, diabetes) were excluded. Additionally, participants were excluded if they had been infected with SARS-CoV-2 less than six months prior or had required hospitalization.

Protocols

Body Composition Assessment

Body mass index (BMI) was calculated using the standard formula: weight (kg)/height^2 (m^2), based on measurements taken with a platform scale equipped with a stadiometer (Filizola, São Paulo, SP, Brazil). Body fat percentage was estimated using the seven-site skinfold protocol by Pollock and Jackson, based on sex and age group, and measured using a Sunny® skinfold caliper. Siri's equation was applied for the final body fat estimation (ISAK, International Society For The Advancement Of Kinanthropometry, 2001; Pollock & Jackson, 1984; Siri, 1993).

Cardiovascular Autonomic Control

To analyze HRV, BPV, and BRS, continuous beat-to-beat recordings were obtained using electrocardiography (lead MC5) and finger photoplethysmography (Finometer system, Finapres Inc.) for arterial pressure measurement. Both systems were connected to a data acquisition unit (PowerLab 4/35, ADInstruments Inc., ML866/P, Australia) and processed using LabChart 8.0 software (ADInstruments). R-R intervals (from electrocardiogram) and systolic blood pressure values (from photoplethysmography) were recorded during 20 minutes of rest in the supine position, followed by 10 minutes in the standing position (active standing test). Laboratory conditions—temperature (22°C), lighting, and noise level—were strictly controlled.

For linear HRV analyses (spectral analysis and root mean square of successive differences, rMSSD), as well as BPV and spontaneous BRS (time-domain spectral analysis and sequence method, respectively), CardioSeries v2.4 software was used (Billman, 2011; Guzzetti et al., 2005; Malliani et al., 1991; Montano et al., 1994; Parati, 2005; Penteado, s. d.; Philbois et al., 2024; TASK FORCE, 1996). For nonlinear HRV analysis, Kubios HRV Standard software (University of Eastern Finland, Kuopio, Finland) was used (Tarvainen et al., 2014). These analyses included Poincaré plots (standard deviations of short- and long-term beat-to-beat variability, SD1 and SD2), approximate entropy (ApEn), sample entropy (SampEn), and detrended fluctuation analysis (DFA) with its short- and long-term exponents (α1 and α2) (Carrasco et al., 2001; Castiglioni & Faini, 2019; Magagnin et al., 2011; Porta et al., 2001; Shaffer & Ginsberg, 2017).

Cardiopulmonary Exercise Testing

Cardiorespiratory fitness was assessed through a submaximal incremental treadmill test (Super ATL Millennium®, Inbramed/Inbrasport, Porto Alegre, RS, Brazil), following a modified Bruce protocol (Bruce, Robert A, 1971; Sheffield & Roitman, 1976). The submaximal HR was defined as baseline HR plus 90% of the heart rate reserve and/or a respiratory exchange ratio (RER) > 1.12, calculated as: HRmax − HRrest. During the test, ventilatory and metabolic parameters (expired volume, oxygen consumption, carbon dioxide production, and anaerobic thresholds I and II) were recorded using the Ultima™ CardiO2 metabolic analyzer (Medical Graphics Corp., St. Paul, Minneapolis, USA).

Statistical Analysis

Sample size was calculated using SigmaPlot® software version 11.0, with a 95% confidence level and 80% power, based on expected differences in normalized units (nu) ofLF and HF variables. Assuming a standard deviation (SD) of 19 and a minimum detectable mean difference of 12, the required sample size was determined to be 41 participants per group.

After initial data screening, Student's t-tests for independent and paired samples were used to compare between and within groups, respectively. When data did not meet normality or homogeneity assumptions, the Wilcoxon signed-rank test (for paired samples) and Mann–Whitney U test (for independent samples) were applied. Statistical significance was set at $p < 0.05$.

Results

The anthropometric characteristics, as well as the hemodynamic and metabolic parameters of participants in both groups, are presented in Table 1. No significant differences were observed between the CONTROL and COVID-19 groups regarding these variables, including VO_2peak (peak oxygen uptake).

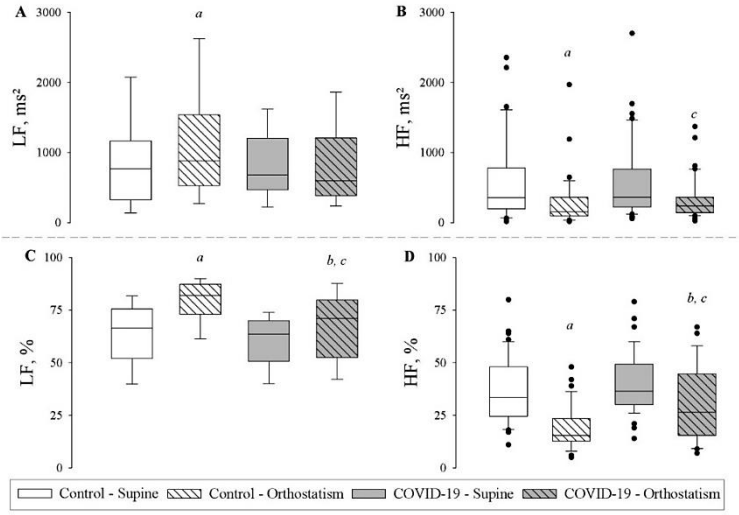
Table 1. Anthropometric characteristics, and metabolic and hemodynamic values obtained in both groups.

	CONTROL	COVID-19	CI 95%	p
Characteristics				
Age, years	43 ± 4	44 ± 6	-0.65 (-2.8;1.5)	0.554
Weight, kg	82 ± 14	86 ± 13	-3.58 (-9.4;2.3)	0.225
Height, m	1.76 ± 0.06	1.74 ± 0.07	0.013 (-0.016;0.04)	0.381
BMI, kg/m^2	27 ± 4	28 ± 3	-1.61 (-3.3;0.11)	0.068
Body fat percentage, %	22.1 ± 6.5	23.7 ± 5.5	-1.65 (4.3;0.9)	0.213
Metabolic and hemodynamic values				
VO_{2peak}, mL/kg/min	33.9 ± 6.4	36.2 ± 7.1	-2.17 (-6;1.2)	0.302
Resting HR, bpm	63 ± 10	66 ± 9	-2.42 (-6.4;1.6)	0.234
SBP, mmHg	120 ± 12	122 ± 13	-2.23 (-7.8;3.4)	0.432
DBP, mmHg	78 ± 11	79 ± 8	-0.97 (-5.6;3.7)	0.682
MBP, mmHg	95 ± 10	96 ± 9	-1.20 (-6;4)	0.424

Values presented as mean ± SD. CI, confidence interval; kg, kilogram; m, meter; kg/m^2, kilogram per square meter; %, percentage; VO_{2peak}, peak oxygen uptake; mL.kg^{-1}.min^{-1}, milliliter per kilogram per minute; bpm, beats per minute; mmHg, millimeters of mercury; BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.

Table 2 and Figure 1 present the results of linear HRV analyses obtained in both the supine and orthostatic positions. In the time-domain analyses, no significant differences were observed between groups in either position. Likewise, spectral analysis in the supine position revealed comparable results between groups. However, during orthostasis, participants in the COVID-19 group exhibited lower low-frequency (LF) oscillations, higher high-frequency (HF) oscillations, and a reduced LF/HF ratio compared to the CONTROL group.

Figure 1. Spectral analysis of heart rate variability in supine and orthostatic positions.



Low-frequency (LF) and high-frequency (HF) oscillations, in absolute and normalized units (nu), and the LF/HF ratio are shown for control and COVID-19 groups during the supine and orthostatic positions. [a] $p < 0.05$ compared to the control group in the supine position; [b] $p < 0.05$ compared to the control group in the orthostatic position; [c] $p < 0.05$ compared to the COVID-19 group in the supine position.

In the CONTROL group, the postural transition (supine to orthostatic) resulted in a reduction in HF oscillations (in both absolute and normalized units), along with an increase in LF oscillations (absolute

and normalized) and in the LF/HF ratio, which are indicatives of sympathetic predominance during orthostatic stress. Similarly, in the COVID-19 group, orthostasis led to a reduction in HF oscillations (absolute and normalized) and an increase in normalized LF oscillations. However, unlike the CONTROL group, the COVID-19 group demonstrated a decrease in overall HRV variance and no change in absolute LF values.

Table 2. Parameters of autonomic modulation of heart rate variability (HRV) obtained in supine and orthostatic positions.

	CONTROL	COVID-19	IC 95%	p
Time Domain				
Supine				
RRi, ms	974 ± 152	933 ± 138	48 (-22;109)	0,187
RMSSD	37 ± 20	39 ± 17	-2,5 (-9,9;4,4)	0,414
Orthostatism				
iRR, ms	810 ± 126 [a]	792 ± 94 [b]	12 (-39;57)	0,619
RMSSD	28 ± 20 [a]	30 ± 13 [b]	-4,4 (-9,3;0,1)	0,054
Spectral analysis				
Supine				
Variance, ms^2	3279 ± 2139	2730 ± 1543	360 (-351;1139)	0,320
LF/HF ratio	2,59 ± 1,75	2,23 ± 1,39	0,22 (-0,37;0,86)	0,447
Orthostatism				
Variance, ms^2	3174 ± 3246	2389 ± 1227 [b]	130 (-433;762)	0,689
LF/HF ratio	6,7 ± 4,4 [a]	4,12 ± 3,70 [b]	2,42 (1;3,8)	<0,001

Values are presented as mean ± standard deviation (SD). RRi, intervals between the R-R waves of the electrocardiogram; ms, milliseconds; RMSSD, square root of the mean square of the differences between adjacent normal RR intervals; SDNN, standard deviation of normal-to-normal R-R-intervals; ms^2 milliseconds squared; LF, low frequency oscillation band (0.04 - 0.15 Hz); HF, high frequency oscillation band (0.15 - 0.4 Hz). [a] $p < 0.05$ compared to the control group in the supine position; [b] $p < 0.05$ compared to the COVID-19 group in the supine position.

Figures 2 and 3 illustrate the results of nonlinear HRV analyses. Figure 2 displays the symbolic and graphical analyses from the Poincaré plots in both supine and orthostatic positions. Both groups showed similar results in most indices, with the exception of the SD2/SD1 ratio, which was lower in the COVID-19 group during orthostasis. Additionally, symbolic dynamics analysis revealed an increase in 0V patterns and a decrease in 2V patterns during orthostasis for both groups. In the Poincaré plot, both groups showed a reduction in SD1 values during orthostasis; however, only the COVID-19 group showed a decrease in SD2 values, while the CONTROL group maintained similar SD2 values across both postures.

Figure 3 presents the results from entropy-based and detrended fluctuation analysis (DFA) in both positions. In the supine position, a significant difference was found only in approximate entropy (ApEn), with the COVID-19 group displaying higher values. During orthostasis, the COVID-19 group exhibited higher ApEn and sample entropy (SampEn) values, along with lower short-term fractal scaling exponent (α1) values. Despite these differences, both groups demonstrated a similar pattern of reduced entropy indices (ApEn and SampEn) and increased DFA parameters (α1 and α2) during orthostasis when compared to the supine position.

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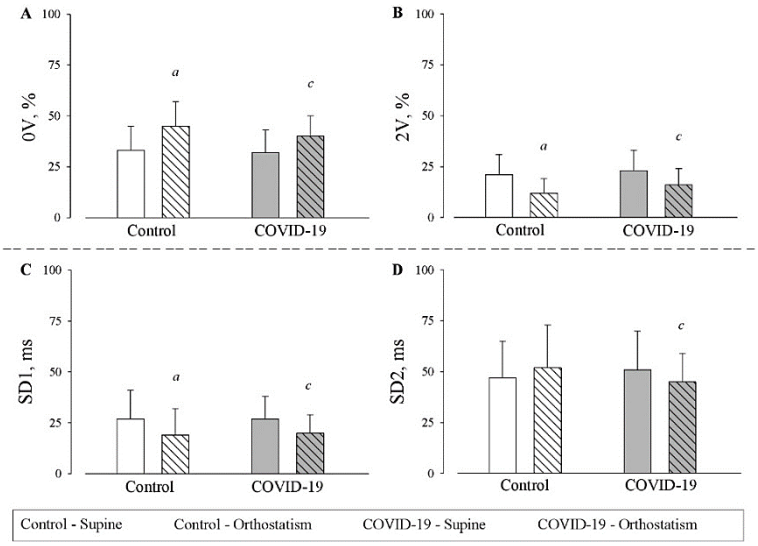
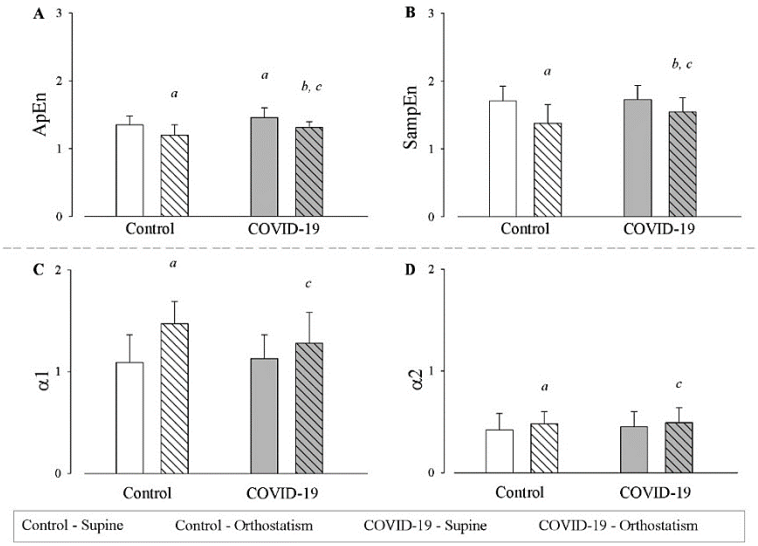
Figure 2. Symbolic and Poincaré plot analysis of HRV in supine and orthostatic positions.



(A) Symbolic analysis shows the percentage of patterns with no variation (0V), and two variations (2V). (B) Nonlinear indices derived from the Poincaré plot: (C) SD1 (short-term variability) and (D) SD2 (long-term variability. [a] $p < 0.05$ compared to the control group in the supine position; [b] $p < 0.05$ compared to the control group in the orthostatic position; [c] $p < 0.05$ compared to the COVID-19 group in the supine position.

Figure 3. Entropy and detrended fluctuation analysis (DFA) of HRV in supine and orthostatic positions.



(A) Approximate entropy (ApEn); (B) sample entropy (SampEn); Detrended Fluctuation Analysis indices (C) α1, short-term scaling; (D) α2: long-term scaling. [a] $p < 0.05$ compared to the control group in the supine position; [b] $p < 0.05$ compared to the control group in the orthostatic position; [c] $p < 0.05$ compared to the COVID-19 group in the supine position.

Table 3 presents the results for BPV and spontaneous BRS for both groups in supine and orthostatic positions. No statistically significant intergroup differences were observed for any of the variables analyzed. In intragroup comparisons, both groups exhibited increased total BPV and LF oscillations in response to orthostasis. Additionally, spontaneous BRS analysis revealed a similar reduction in the number of baroreflex sequences and baroreflex gain in both groups during the orthostatic condition.

Table 3. Analysis of blood pressure variability and spontaneous baroreflex sensitivity in both groups during supine and orthostatic positions

	CONTROL	COVID-19	CI 95%	p
Blood Pressure Variability				
Supine				
Variance, mmHg²	27 ± 12	29 ± 17	-1.3 (-6.5;3.4)	0.580
LF, mmHg²	7.9 ± 5.4	9.0 ± 4.7	-1.44 (-3.2;0.3)	0.107
Orthostatism				
Variance, mmHg²	41 ± 18 [a]	49 ± 26 [b]	-4 (-13;3)	0.303
LF, mmHg²	21.8 ± 12.8 [a]	19 ± 10.4 [b]	2.07 (-2.5;7)	0.371
Spontaneous baroreflex sensitivity				
Supine				
BEI	0.59 ± 0.16	0.53 ± 0.17	0.05 (-0.02;0.1)	0.160
Ramps, nº	128 ± 41	117 ± 56	12.0 (-9;33)	0.271
Up, ms/mmHg	14.1 ± 8.6	12.8 ± 5.9	0.3 (-2;3)	0.763
Down, ms/mmHg	14.0 ± 7.8	12.7 ± 5.5	0.62 (-2.1;3.2)	0.763
Gain total, ms/mmHg	14.0 ± 7.9	12.8 ± 5.5	0.46 (-2;3)	0.770
Orthostatism				
BEI	0.58 ± 0.17	0.55 ± 0.18	0.03 (-0.05;0.1)	0.454
Ramps, nº	79 ± 27 [a]	86 ± 35 [b]	-6.0 (-19;6)	0.299
Up, ms/mmHg	8.5 ± 4.8 [a]	7.5 ± 2.9 [b]	0.36 (-0.9;1.7)	0.612
Down, ms/mmHg	8.1 ± 3.7 [a]	8.3 ± 2.8 [b]	-0.44 (-1.6;0.8)	0.382
Gain total, ms/mmHg	8.3 ± 4.2 [a]	8.0 ± 2.8 [b]	-0.2 (-1.4;1.1)	0.741

Values presented as mean ± SD. CI, confidence interval; mmHg, millimeter of mercury; LF, low frequency; BRS, baroreflex sensitivity; BEI, baroreflex effectiveness index; ms/mmHg, milliseconds/millimeter of mercury; gain up, increase in the pulse interval (bradycardia) resulting from increased blood pressure, gain down, reduction in the pulse interval (tachycardia) resulting from a reduction in blood pressure. [a] p < 0,05 vs. control group in supine position; [b] p < 0,05 vs. COVID-19 group in supine position. [a] p < 0.05 compared to the control group in the supine position; [b] p < 0.05 compared to the COVID-19 group in the supine position.

Discussion

The present study investigated the long-term effects of mild COVID-19 infection on cardiovascular autonomic modulation in middle-aged men, with a focus on HRV, BPV, and BRS. Although no differences were observed between groups in anthropometric, hemodynamic, or metabolic parameters, notable alterations were found in the autonomic response to orthostatic stress.

At rest (supine position), both groups showed similar autonomic parameters, including time and frequency domain indices of HRV, as well as BPV and BRS measures. These findings suggest that baseline autonomic modulation remains largely preserved in individuals recovering from mild COVID-19. However, the transition to the standing position revealed a distinct autonomic profile in the COVID-19 group, characterized by lower absolute LF oscillation values in spectral analysis, reduced SD2 values in Poincaré plot analysis, and decreased LF/HF ratio and overall HRV variance. Although LF and LF/HF do not provide a direct measure of sympathetic activity, the blunted increase in LF during orthostatic challenge in the post-COVID group, along with their lower LFnu and LF/HF compared with controls, may indicate a less pronounced autonomic adjustment to postural change (Jacob et al., 2019).

Although direct comparison of absolute values is limited by differences in protocols and analytical approaches across studies, the magnitude of autonomic alterations observed in our study is comparable to those reported by da Silva et al. (2023), who examined post-COVID patients using passive tilt-table testing. In their sample, LF increased by only 5% during orthostasis, whereas healthy controls exhibited a substantially larger increase (10%). In our study, although the orthostatic challenge was milder (active standing), we observed a similarly attenuated LF response in the post-COVID group (from 60% to 70%), while controls showed a more pronounced increase (from 63% to 81%). A similar pattern was observed for SampEn: in da Silva et al., the COVID-19 group started with lower baseline SampEn and showed a marked reduction during tilt, converging toward control values. In contrast, our participants exhibited comparable baseline SampEn across groups, but the post-COVID group demonstrated a smaller decrease during standing, indicating a blunted autonomic adjustment despite preserved resting complexity.

This blunted autonomic adjustment may reflect impairments in either central or peripheral components of the ANS, including baroreflex pathways and central autonomic nuclei, structures previously implicated in the pathophysiology of COVID-19 and long COVID (Aghagoli et al., 2021; Chu et al., 2020; Fedorowski et al., 2024). Our findings are consistent with previous reports of autonomic imbalance following

COVID-19 infection (Al-kuraishy et al., 2021; Asarcikli et al., 2022; Dani et al., 2021). However, we expand upon existing evidence by demonstrating that even individuals who experienced mild, non-hospitalized COVID-19 infections may present with persistent autonomic alterations months after recovery.

Nonlinear analyses further support these findings. Increased ApEn and SampEn values in the COVID-19 group, both at rest and during orthostasis, indicate greater signal irregularity and diminished autonomic organization. Moreover, the reduced short-term fractal scaling exponent (α1) during orthostasis suggests decreased complexity and adaptability of short-term autonomic control (Mäkikallio et al., 2001; Silva et al., 2017). These markers of disorganization have previously been described in populations with autonomic dysfunction and may reflect impaired integration of central and peripheral autonomic inputs (Rafanelli et al., 2019).

Interestingly, while both groups exhibited the expected sympathetic activation in response to standing — namely, decreased HF and increased LF components — the COVID-19 group failed to show an increase in absolute LF oscillations, and instead demonstrated reduced total HRV variance. Together with the lower SD2 and SD2/SD1 ratio, these findings reinforce the hypothesis of impaired sympathetic mobilization in response to orthostatic stress.

BPV and BRS analyses did not reveal intergroup differences, and both groups showed the expected responses to orthostasis. However, the combined evidence from spectral and nonlinear HRV analyses suggests a degree of autonomic dysregulation that may not be fully captured by BPV and BRS measurements alone. These findings highlight the importance of including multiple autonomic markers, as HRV analysis may detect subtle dysfunctions not captured by BPV or BRS alone.

The pathophysiological mechanisms underlying these findings are likely multifactorial. It is well-established that SARS-CoV-2 exhibits neurotropic properties and may affect brain regions involved in autonomic regulation, including the brainstem and insular cortex (Yachou et al., 2020). Additionally, low-grade chronic inflammation, endothelial dysfunction, and immune-mediated mechanisms may contribute to autonomic imbalance in the post-acute phase of infection (Hadaya & Ardell, 2020; Idris Fadul et al., 2025).

From a clinical perspective, persistent impairments in autonomic responsiveness — even in individuals with mild disease — are concerning, as they may increase susceptibility to cardiovascular events (Thayer et al., 2010). These findings underscore the importance of long-term monitoring of autonomic function in post-COVID-19 individuals, regardless of the initial severity of infection.

This study has several limitations. First, data collection occurred at different time points: before the pandemic for the control group, and after for the COVID-19 group. Nonetheless, strict methodological consistency was maintained, including the same data collection site, equipment, and team. Second, the study sample consisted exclusively of male participants. Women were excluded due to known physiological differences in cardiac autonomic modulation between sexes, which could have introduced methodological bias (Dutra et al., 2013; Facioli et al., 2018). However, this limits the generalizability of our findings to women and physically active individuals. Additionally, the cross-sectional design precludes causal inference, and no inflammatory or immune biomarkers were assessed to support the proposed mechanisms. Finally, although care was taken to match the groups and minimize methodological bias, unmeasured variables such as psychological status or subclinical inflammation may have influenced autonomic function.

Future studies should adopt longitudinal designs to track the progression of autonomic recovery over time and include biomarkers of neural and vascular inflammation. Expanding the sample to include diverse age groups, sexes, and physical activity levels will also help clarify the broader implications of these findings.

Conclusions

This study demonstrates that individuals recovering from mild, non-hospitalized COVID-19 may present with persistent autonomic dysfunction, particularly a blunted autonomic adjustment to orthostasis. These findings underscore the subtle but clinically relevant impact of SARS-CoV-2 on cardiovascular

autonomic regulation and the importance of ongoing clinical and scientific attention to post-COVID-19 outcomes.

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